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Clinical Impact of Somatostatin Receptor Scintigraphy in the Management of Patients with Neuroendocrine Gastroenteropancreatic Tumors

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Somatostatin receptor scintigraphy (SRS) has been used for the detection of gastroenteropancreatic (GEP) tumors. This study evaluates the clinical impact of SRS in GEP tumor detection and its therapeutic implications on patient management. **Methods:** We prospectively studied 160 patients with biologically and/or histologically proven GEP tumors. Before SRS, patients were classified into three groups: gastrointestinal (Group 1; n = 90) patients without known metastases; (Group 2; n = 59) patients with metastases limited to the liver; (Group 3; n = 11) patients with known extrahepatic metastases. The scintigraphic data were compared to the radiological findings. **Results:** In Group 1, without known metastases, conventional imaging detected 53 primary sites in 44 patients: SRS was positive in 68% of these sites and discovered 4 additional primary tumors in 3 patients and 16 metastases in 14 patients. Conventional imaging was negative in 46 patients: SRS discovered 47 new sites in 36 patients. In Group 2, SRS confirmed liver metastases in 95% of patients and discovered 45 new sites in 36 of these patients. In Group 3, SRS disclosed 11 new sites in 7 patients. These results modified patient classification in 38 cases (24%). Surgical therapeutic strategy was changed in 40 patients (25%). **Conclusion:** Somatostatin receptor scintigraphy improves tumor detection, has major clinical significance and should be performed systematically for staging and therapeutic decision making in patients with GEP tumors.

Key Words: somatostatin receptor scintigraphy; gastroenteropancreatic tumors; neuroendocrine tumors

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Gastroenteropancreatic (GEP) neuroendocrine tumors are slow-growing tumors, clinically silent for many years and often detected when metastases have developed, most commonly in the liver (*1,2*). Tumor localization is essential since surgery remains the optimal treatment in most patients without metastases (*3–6*). Curative surgery is difficult since primary tumors are frequently very small (<1 cm) and potentially undetectable by conventional imaging. Therefore, patients commonly relapse, suggesting the presence of undetected residual tumors. When liver metastases occur, the staging of these patients is essential for therapeutic management. Additional procedures such as hepatectomy, hepatic artery chemoembolization or even liver transplantation in very selected cases can be proposed in patients with metastases limited to the liver. In case of extrahepatic metastases, chemotherapy and more recently octreotide therapy are most frequently indicated. Tumor localization for accurate staging and therapeutic management justifies the use of new imaging techniques such as endoscopic ultrasonography (EUS) (*7,8*) and somatostatin receptor scintigraphy (SRS) (*9,10*).

SRS has been previously reported as an accurate tool for the detection of neuroendocrine tumors (*11,12*), based on the presence of high-affinity binding sites for somatostatin receptor (*13–16*). The aim of our study was to evaluate prospectively the additional clinical value of SRS and its implication on therapeutic management as compared with conventional imaging in patients with GEP tumors, including EUS, for the investigation of the duodenopancreatic area.

MATERIALS AND METHODS

Patients

The impact of SRS was analyzed in 160 consecutive patients (72 women and 88 men, mean age 52 ± 3 yr) with proven GEP tumors, seen in our institution from November 1992 to September 1995. The study population included 78 patients with Zollinger–Ellison syndrome (ZES), 38 patients with a carcinoid tumor and 44 patients with other types of neuroendocrine tumors. Diagnosis of ZES was based on histopathology and specific biological syndrome (n = 60) or only specific biological syndrome (n = 18). In all of the patients with carcinoid tumors and other neuroendocrine tumors, the diagnosis was histologically confirmed. All together, histological confirmation of tumors was obtained in 142 of 160 patients.

Of the 160 patients, 108 were investigated in the primary staging of GEP tumors. Fifty-two patients were investigated for clinical

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and/or biological recurrence of disease (27 ZES, 25 carcinoid) 4 ± 1 yr after surgery.

Twelve patients were treated by octreotide prior to SRS: in all but three patients octreotide was stopped 3 days before and during SRS. In these three patients, octreotide was not stopped.

Follow-up was conducted for 100 patients (mean time after SRS 18 ± 2 months, range: 4–36 mo). Fifty patients underwent another SRS, and surgery was performed in 30 patients.

Conventional imaging included chest radiographs, contrast-enhanced abdominal computed tomography (CT) and abdominal ultrasonography in all patients. Magnetic resonance imaging of the abdomen was performed in 17 patients and abdominal angiography in 9 patients. EUS was proposed each time an accurate investigation of the duodenopancreatic area was feasible (in particular, absence of previous abdominal surgery) or clinically relevant (patients with ZES, nonclassified GEP tumors and patients without an already detected large primary tumor and/or diffuse metastases). Hence, EUS of the duodenopancreatic area was performed in 59 patients.

To evaluate the additional value of SRS in patient management, patients were classified into three groups according to the presence or absence of liver and/or extrahepatic metastases on the basis of conventional imaging results, before SRS. Group 1 included 90 patients without detected metastases, Group 2 included 59 patients with metastases limited to the liver and Group 3 included 11 patients with known extrahepatic metastases.

Because 21 ZES patients in Group 1 were submitted to surgical resection of the primary tumor, an accurate comparison between SRS and EUS results was done.

Tumor detection rates in ZES, carcinoid and other types of tumors were expressed as the percentage of patients with positive sites and compared using the χ^2 test ($p < 0.05$ was considered significant).

Somatostatin Receptor Imaging

A digestive preparation including a 3-day low residue diet and a 24-hr laxative procedure was applied before SRS imaging to decrease undesirable bowel activity.

Indium-111-DTPA-D-PHE1-octreotide (135 MBq) was administered immediately after checking the specific radiochemical purity by chromatography, which was always higher than 95%. No adverse reaction was observed in the whole series.

Scintigraphic images were acquired using a single-head circular large field of view rotating gamma camera or a double-head camera with a medium resolution parallel-hole collimator using a 256 × 256 word matrix with a preset time of at least 10 min. Acquisition was adjusted to both ^{111}In photopeaks (171 and 245 keV). Abdominal images were obtained at 4 hr after injection, in the anterior and posterior views. At 24 hr, the acquisition included systematically anterior and posterior views for the head, chest and pelvis, and anterior, posterior, lateral and oblique views for the abdomen. Additional lateral or oblique views of the chest or head were performed when necessary. Delayed images were systematically done for the abdomen in the anterior and posterior views at 30–48 hr after injection. In case of negative or doubtful images, the acquisition time was increased from 15–20 min.

Abdominal SPECT was performed in 64 patients to prospectively and comparatively evaluate planar and SPECT images. Acquisition parameters were a double indium peak acquisition, 64 projections over 360° rotation, 60 sec per step, 64 × 64 matrix. Slices were reconstructed after backprojection using a Hann filter.

Scintigraphic images were visually analyzed by two blinded independent observers. Disagreements were resolved by consensus. A comparison of scintigraphic and radiological findings was performed for each tumoral site.

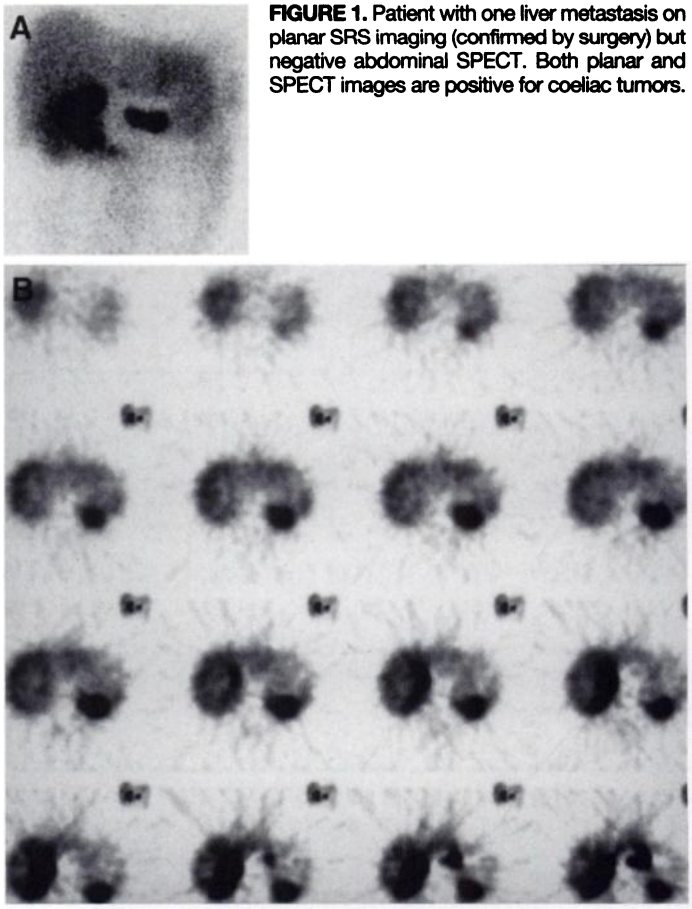

FIGURE 1. Patient with one liver metastasis on planar SRS imaging (confirmed by surgery) but negative abdominal SPECT. Both planar and SPECT images are positive for coeliac tumors.

RESULTS

Technical Considerations

Four-hour images provided tumor visualization in the liver, which were missed by 24-hr images in only 2/160 patients. Conversely, six sites corresponding to four patients were only evidenced by 24 hr images.

Lateral and oblique views provided additional information in 11 patients: 6 liver, 3 abdominal and 2 rib tumors were visualized only by these views.

Abdominal SPECT, compared with planar images, detected eight additional sites in three patients and provided better visualization in one patient. Twenty-one tumoral sites in 9 patients were detected by planar imaging but were missed by SPECT (12 liver, 7 duodenopancreatic and 2 lower abdomen) (Fig. 1).

The primary tumor detection rate seems to be related to the tumor size. Considering the size of the 28 primary tumors removed by surgery (range: 3–30 mm), the SRS detection rate was 6/16 (38%) for tumors of less than 10 mm and 11/12 (92%) for tumors larger than 10 mm.

Global Detection Rate

Conventional imaging including EUS was positive in 114 of the 160 patients (71%), as summarized in Tables 1 and 2. SRS was positive in 125 patients (78%). More interestingly, SRS was positive in 28 of the 46 patients with previously undetected tumors on the basis of conventional imaging (61%), whereas SRS was negative in only 17 of the 114 patients (15%) with known tumor sites. A few large tumor sites (n = 3), more than 2 cm and 3 cm were SRS negative. Thus, SRS provided additional detection sites compared with conventional imaging even if the global detection rate (78% versus 71%) was quite similar. The detection rate was not significantly different

TABLE 1
Comparison of SRS Versus Conventional Imaging in the Detection of Primary Tumor Sites

Overall population (160 patients)	SRS positive	
	Known sites	New sites
Conv imag positive: 70 (84)	51 (61)	27 (33)
Conv imag negative: 90 (0)		17 (22)

Results are expressed as the number of patients and, in parentheses, as the number of sites. Conv imag = conventional imaging; SRS = somatostatin receptor scintigraphy.

considering the type of GEP tumors: 77%, 75% and 64% of the primary tumor sites were positive, and 92%, 81% and 93% of the metastatic sites were positive in, respectively, ZES, carcinoids and other types of neuroendocrine tumors.

In the overall population of 160 patients, 111 new sites were discovered by SRS in 80 patients. Thirty-seven of these 111 sites (12 in the coeliac area, 3 in the liver, 9 in the chest, 10 in the bone, 3 in the abdomen) were confirmed during follow-up either by conventional imaging and/or by surgical findings in 30 patients. Additional tumor sites discovered by SRS in patients with previously proven metastatic lesions were not further explored (n = 17). Follow-up results are not yet available for the remaining 29 patients.

In the duodenopancreatic area in the 21 patients with surgical confirmation, SRS was positive in 51% of the patients, and EUS was positive in 51% of the patients, whereas the combination of SRS and EUS was positive in 90% of patients. In contrast, CT was positive in only one patient.

In the three patients having SRS while receiving octreotide therapy, SRS was positive confirming known tumor sites and discovering new sites.

Results in Patients Groups

Group 1. In this group (90 patients without known metastases), both localization of the primary tumor site and the detection of unknown metastases are crucial (Table 3).

Of the 90 Group 1 patients, conventional imaging detected 53 primary sites in 44 patients. SRS detected 36 of these 53 sites in 30 of these patients (68%) and discovered 4 additional primary sites in 3 patients and 16 metastatic sites in 14 patients (Fig. 2). Forty-six patients had no detectable tumors by conventional imaging despite clinical and biological indications of GEP tumors. Among these 46 patients, SRS revealed 22 primary tumors in 17 patients.

Among these 90 patients without previously known metastases, 29 metastatic sites were discovered by SRS in 25 patients (28%): 21 extrahepatic sites in 17 patients, 7 liver metastases in 7 patients and 1 liver and 1 extrahepatic metastase in 1 patient.

TABLE 2
Comparison of SRS Versus Conventional Imaging in the Detection of Metastatic Sites

Overall population (160 patients)	SRS positive	
	Known sites	New sites
Conv imag positive: 70 (75)	65 (67)	21 (27)
Conv imag negative: 90 (0)		25 (29)

Results are expressed as the number of patients and, in parentheses, as the number of sites. Conv imag = conventional imaging; SRS = somatostatin receptor scintigraphy.

TABLE 3
Comparison of SRS Versus Conventional Imaging Results in the Detecting Tumor Sites in Group 1 Patients

Group 1 (90 patients)	SRS positive		
	Known sites	New primary sites	New metastases
Conv imag positive: 44 (53)	30 (36)	3 (4)	14 (16)
Conv imag negative: 46 (0)	0	17 (22)	11 (13)

Results are expressed as the number of patients and, in parentheses, as the number of sites. Conv imag = conventional imaging; SRS = somatostatin receptor scintigraphy.

Finally, in the overall group, SRS discovered 26 additional unknown primary lesions in 20 patients and 29 metastatic sites in 25 patients.

Group 2. This group included 59 patients with known metastases limited to the liver using conventional imaging. SRS confirmed these metastases in 56 patients (95%) and detected new liver sites in 5 patients. SRS discovered 18 extrahepatic metastases in 13 of 59 patients (22%) (Fig. 3).

Nineteen patients had 22 known primary tumors and/or tumoral local lymph nodes: 17 of 22 sites (77%) were detected by SRS in 15 patients (79%). In addition, SRS discovered 22 primary tumors in 20 patients. Globally, SRS discovered 45 new sites concerning 36 patients.

Group 3. SRS confirmed 19 of 25 known tumor sites: 8 of 9 primary tumor sites in 6 patients and 11 of 16 known metastatic sites in 8 patients. SRS missed five tumor sites in three patients: two in the lung and three in the abdomen.

In addition, SRS discovered seven new sites in the duodenopancreatic area in four patients and four new metastatic sites (one cervical lymph node, two thoracic, one bone) in three patients.

Finally, SRS discovered 11 new sites in 7 patients (64%).

Implications on Patient's Classification and Therapeutic Strategies

SRS findings modified patient classification in 38 (24%) and changed surgical strategies in 40/160 patients (25%).

Group shifts are summarized in Table 4. Seven patients shifted from Group 1 to Group 2: in six patients SRS showed only one liver metastasis, and curative surgery of the primary

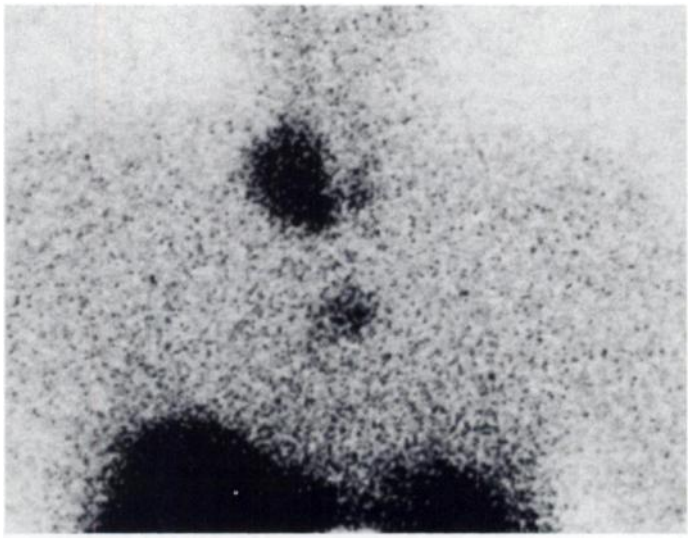

FIGURE 2. Group 1 patient with ZES. SRS discovered mediastinal tumor confirmed only 1 yr later by CT and surgery as a thymic tumor.

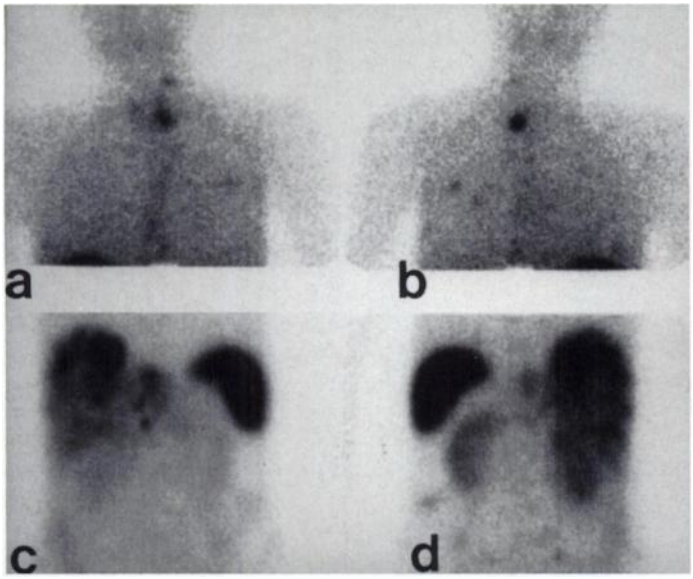

FIGURE 3. (a) Anterior view. (b) Posterior view of the chest. (c) Anterior and (d) posterior view of the abdomen of Group 2 patient with known liver metastases. SRS discovered bone metastases.

tumor associated to liver surgery could be indicated. In one patient, liver metastases were diffuse and only chemotherapy could be proposed. Eighteen patients shifted from Group 1 to Group 3.

In Group 2, SRS revealed extrahepatic metastases in 13 patients: these patients shifted from Group 2 to Group 3 and a curative surgery was contraindicated. Among these patients, a previous decision of liver transplantation was thereafter declined in three patients. In two other patients SRS did not entail any change in group location, but SRS discovered in these patients new liver metastases (controlateral in one patient and diffuse in the other one) precluding liver surgery.

Surgery was performed after SRS in 30 patients: the primary tumor was removed in 24 patients (21 ZES, 3 nonclassified tumors), mediastinal tumor in 1 patient (ZES), liver tumor in 4 patients, and in 1 patient with liver metastases (1 carcinoid), the primary tumor only was removed. Of the 24 ZES patients without known metastases, surgery found 28 tumors in 22 patients: CT was positive in 3 of 22 patients, EUS in 11 of 19 and SRS in 14 of the 22 patients. The primary site localization was found only by SRS in seven patients. In another patient, SRS showed four primary sites as compared to only two sites detected by EUS. The surgeon found and removed only two sites. However, a second surgery was necessary 4 mo later because of a persistent biological syndrome and SRS hot spots. SRS and biology normalized thereafter. Five patients with liver metastases had surgery: liver surgery (n = 2), liver and primary tumors or lymph nodes (n = 2) and only surgery of the primary tumor (n = 1) were performed. In these patients, CT and SRS were positive in all cases of liver metastases. For primary tumors, CT was positive in two patients, and SRS was positive in all patients. In the last patient without known metastases (ZES), SRS discovered a mediastinal abnormal uptake, confirmed by a second SRS 1 yr later and by CT and surgery 2 yr later: This patient had mediastinal surgery for a neuroendocrine thymic tumor.

TABLE 4
Group Shifting of Patients After SRS Findings

Before SRS	Group 1 (90 patients)	Group 2 (59 patients)*	Group 3 (11 patients)
From Group 1 to Group 2	→	7 patients	
From Group 1 to Group 3	→		18 patients
From Group 2 to Group 3		→	13 patients
After SRS	65 patients	53 patients	42 patients

*Two patients were in Group 2: SRS discovered unsuspected controlateral or diffuse liver sites precluding hepatectomy.

DISCUSSION

Our results demonstrate that SRS, as compared with conventional imaging, provides major additional information with important clinical implications since patient classification was modified in 24% of cases and surgical strategies in 25% of cases.

Most neuroendocrine GEP tumors express a high density of somatostatin receptors (*13–16*). Indium-111-pentetreotide scintigraphic imaging has been successfully used to image GEP tumors (*17–24*). Pentetreotide tumoral uptake is mostly related to the density of somatostatin receptors and their affinity for the radioligand, which explains the variable response of SRS from one patient (or from one tumor site) to another (*13,14,16*).

In our study, SRS seems to be very accurate, visualizing 84% of 196 tumor sites detected by conventional imaging and discovering 111 unsuspected new tumor sites in 50% of the patients. These results are in agreement with other previously published reports. Lamberts et al. (*10–14*), Krenning et al. (*9,11,17,20*) and Kwekkeboom et al. reported positive findings in 60%–90% of the patients with GEP tumors and detected new tumor sites in 33% of the patients. Jamar et al. (*25*) reported a higher detection rate with SRS (87%) when compared with that obtained with conventional imaging (82%). Similar results were found by other authors (*26–30*). The results of the European Multicenter Trial reported that SRS visualized 297 of 388 known sites and revealed 166 unsuspected lesions in 308 patients; 40% of these unsuspected lesions were subsequently confirmed as true-positive. In our study, 37 of 111 unsuspected sites were confirmed as true-positive. One limitation of our study was that several additional sites discovered by SRS were not further investigated in patients with previously proven metastatic lesions for ethical considerations, since the confirmation of these lesions would not have changed the patient's management. However, in those patients for whom follow-up results were available, histological data or conventional imaging confirmed 37 lesions in 30 patients, sometimes 1–2 yr later. Two tumor sites in two ZES patients were not found at surgery and therefore not confirmed; in one patient, a repeated SRS remained positive, and the biological syndrome persisted after surgery, suggesting residual tumor tissue. The global results suggest high sensitivity, specificity and early positivity of SRS in the detection of GEP tumors.

Some particular interests and limitations points of SRS must be emphasized. For SRS and conventional imaging, 95/160 (60%) of the patients had metastases. Moreover, 28% of Group 1 patients had metastases despite early diagnosis and small primary tumor size. This suggests that tumoral extension may be underestimated in the staging of GEP tumors that did not include SRS, therefore penalizing the potential benefit of surgery. Interpretation of radiological imaging is often difficult for the duodenopancreatic area, especially after previous surgery; SRS imaging may facilitate radiologic interpretation. SRS is particularly efficient for tumors larger than 10 mm, with a detection rate of 92%, in contrast to 38% for tumors less than 10 mm. In this area the combination of SRS and EUS seems to be the most effective procedure, since it detects 90% of primary

tumors as already shown in the 21 patients with ZES who had surgery after SRS. SRS tumor detection is also dependent on the density of somatostatin receptors independently (some large tumor sites more than 2 or 3 cm were missed by SRS). The detection rate is not different according to the histologic type of neuroendocrine tumor.

In the 52 patients who had previous surgery, SRS results were quite similar to those of patients without previous surgery. SRS was negative in 14/52 patients and discovered new tumors in 20/52 patients. Patient classification was changed in 14/52 patients (27%) (12 patients moved from Group 1 to Group 3 and two patients from Group 1 to Group 2). In patients without prior surgery (n = 108), patient classification was changed in 24/108 (22%) (ns).

The demonstration of new tumor sites by SRS greatly affected impact on therapeutic decision. In our series, these results led to a change in the classification of patients and to modifications in therapeutic management in 25% of the patients because of the discovery of unsuspected liver tumors in 7 patients, controlateral liver tumors before hepatectomy in 2 patients and evidencing extrahepatic metastases in 31 patients. In the results obtained from the European Multicenter Trial and reported in 235 patients, the information provided by SRS affected surgical decisions in 29 patients; surgery was undertaken in 21 patients and canceled in 8, whereas octreotide therapy was initiated in 47 patients, as reported by other authors (*31–34*). Jamar et al. (*25*) reported that SRS findings guided the therapeutic decision in 20 of 38 patients (53%); multiple tumor sites were discovered by SRS in 5 of 16 patients (31%) considered as having a single or no known lesion, thus contraindicating curative surgery. In patients who were candidates for surgery (on the basis of conventional imaging methods), SRS may confirm the therapeutical plan when no additional tumor sites are visualized with SRS.

Conventional imaging is useful in the diagnosis and the better anatomical localization of GEP tumors, whereas the information provided by SRS is essential for therapeutic decision and underlines the importance of performing SRS for staging. The usefulness of SRS as a first-line procedure was analyzed retrospectively. Patients were classified into three groups according to the presence or absence of liver and/or extrahepatic metastases on the basis of SRS results. Group 1 included 71 patients without metastases. Group 2 included 50 patients with metastases limited to the liver and Group 3 included 39 patients with extrahepatic metastases. Conventional imaging analyzed after SRS changed patient classification in only six patients (4%): three patients moved from Group 1 to Group 2, and three patients moved from Group 1 to Group 3. Conventional imaging changed surgical strategies in 6/160 patients (4%).

SRS should be proposed as a first-line investigation for the staging of patients. In the case of extrahepatic, extra-abdominal metastases demonstrated by SRS, no additional procedures are required for patient management. Before a surgical cure, SRS seems very helpful because it may increase the detection rate and improve primary tumor localization, ensuring a complete cure and thus providing a better chance to prevent recurrence of the disease. To improve localization and complete resection of tumors during surgery, other studies reported a potential interest of intraoperative use of a labeled octreotide (*35*). In patients with known liver metastases, in whom either liver artery chemoembolization, hepatectomy or transplantation are potentially indicated, SRS is crucial in confirming these indications. In our population, liver transplantation was contraindicated in three patients because of extra-abdominal metastases, leading to major medical and economic relevance.

It must be emphasized that these positive results may also be dependent on the acquisition method, thereby requiring long-time planar images and multiple abdominal views repeated at three different times. The best compromise for tumor detection were 24-hr images. However, obtaining earlier images was also helpful in the abdomen, providing easier detection when the tumor-to-physiological uptake ratio was higher due to low physiological accumulation in the liver and kidneys and the absence of bowel uptake. Abdominal images obtained later (30–48 hr) were also helpful in differentiating tumoral from digestive tracer uptake, which may be increased even if patient preparation was adequate.

Abdominal SPECT may provide additional information with regard to tumor localization and to differentiate specific uptake from bowel activity. However, it presents a lower diagnostic value as compared with the whole set of planar images, which cannot be substituted by SPECT.

CONCLUSION

Indium-111-pentetreotide scintigraphy is a sensitive and accurate procedure for the imaging and staging of GEP tumors. Somatostatin receptor scintigraphy may be proposed as a first-line investigation in patients with clinical and biological diagnosis of GEP tumors by selecting patients eligible for curative surgery from those with extrahepatic metastases. In patients without extrahepatic metastases demonstrated by SRS, conventional imaging may be useful to confirm surgical indication. In these patients, the association of EUS and SRS is powerful for detecting and localizing primary tumor sites. The accuracy of SRS depends on the acquisition of multiple views, including lateral and oblique views and/or SPECT. Conversely, conventional imaging alone is not accurate enough for detecting hepatic and extrahepatic metastases, underestimating the tumoral extension in nearly one-third of the patients. Thus, our results suggest that SRS is required for the preoperative management of patients with GEP tumors.

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Phase I/II Clinical Radioimmunotherapy with an Iodine-131-Labeled Anti-Carcinoembryonic Antigen Murine Monoclonal Antibody IgG

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The aim of this study was to determine, in a Phase I/II clinical trial, the pharmacokinetics, dosimetry and toxicity, as well as antitumor activity, of the ^{131}I-labeled murine anti-carcinoembryonic antigen (CEA) monoclonal antibody, NP-4 (IgG_1 subtype). **Methods:** A total of 57 patients with CEA-expressing tumors (29 colorectal, 9 lung, 7 pancreas, 6 breast and 4 medullary thyroid cancer patients), mostly in very advanced stages, were treated. The patients underwent a diagnostic study (1–3 mg of IgG and 8–30 mCi of ^{131}I) to assess tumor targeting and to estimate dosimetry, followed by the therapeutic dose (4–23 mg and 44–268 mCi), based on the radiation dose to the red marrow. Imaging was performed from 4–240 hr postinjection (planar and SPECT). Blood and whole-body clearance were determined; radiation doses were calculated by the Medical Internal Radiation Dose scheme. **Results:** Red marrow doses ranged from 45 to 706 cGy, and whole-body doses ranged from 31 to 344 cGy. Differences in pharmacokinetics were found between different types of CEA-producing tumors: blood $T^{1/2}$ was significantly lower in colorectal cancer when compared to all other tumor types (21.4 ± 11.1 hr versus 35.8 ± 13.2 hr; $p < 0.01$), as was also whole-body $t_{1/2}$. Myelotoxicity was dose-limiting, and its severity was related to the types of prior therapy and extent of bone marrow involvement. In patients without prior radiation or chemotherapy, marrow doses as high as 600 cGy were tolerated without evidence of dose-limiting toxicity. No major toxicity to other organs was observed. Tumor doses were inversely related to the tumor mass and ranged between 2 and 218 cGy/mCi. Modest antitumor effects were seen in 12 of 35 assessable patients (1 partial remission, 4 minor/mixed responses and 7 with stabilization of previously rapidly progressing disease). **Conclusion:** These results suggest that prior chemotherapy or external beam radiation is an important risk factor for the development of hematological toxicity in radioimmunotherapy and that higher radiation doses may be delivered to tumors of patients without prior therapy compromising the bone marrow reserve. The different and, in the individual cases, unpredictable clearance rates suggest the necessity of dosimetry-based treatment planning rather than mCi/m^2 dosing. Small tumors seem to be more suitable for radioimmunotherapy because of their favorable dosimetry, but to achieve better therapeutic results in patients with bulky disease, the application of higher, potentially myeloablative doses is indicated.

Key Words: radioimmunotherapy; iodine-123-anti-CEA; pharmacokinetics

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Carcinoembryonic antigen (CEA)-expressing adenocarcinomas occur in the most frequent types of cancer, including colorectal, lung and breast cancers (*1*). Although there have been advances in the surgical management of primary tumors, rendering surgery possible in certain more advanced stages of disease, the major cause of cancer mortality is the spreading of the disease to distant sites (*2*). The three conventional treatment strategies, i.e., surgery, external beam radiation and chemotherapy, are only of limited value in the management of metastatic disease (*2*). Furthermore, chemotherapy is burdened by multiorgan toxicity, often compromising the patient's quality of life (*2*).

There has been an increasing emphasis on the recognition of

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